REMARKS

Claims 22 and 24-35 are pending for consideration in the instant application upon entry of the present Amendment. Claims 1-90 were pending and claims 1-21, 37, 39, and 41-90 have been withdrawn from consideration in the instant application as being drawn to non-elected subject matter. In response to the Examiner's comments regarding duplicate numbering of claims, the claims have been renumbered to correct these errors and are now numbered 1-91 instead of 1-90 as originally listed in the specification as filed. Claims 23 and 36-40 have been canceled without prejudice to pursuing the claimed subject matter in other applications.

Claims 22 and 24-28 have been amended to more particularly and distinctly claim the subject matter of the present invention. The claim amendments are fully supported by the application as originally filed (*see, e.g.,* the instant application at Example 1 on pages 21-22), and do not represent new matter. The abstract of the instant application has been amended, as reflected on page 2 of the present Amendment, to include a concise statement of the technical disclosure of the patent. No new matter has been added.

Applicants submit herewith a Supplemental Information Disclosure Statement with references A04 to A50, B01 to B18 and C01 to C38. The majority of cited references were also cited in copending U.S. Patent Application No. 09/606,909. None of the references cited in the Supplemental Information Disclosure Statement disclose the subject matter of the instant application. While some of the references may disclose delivery of α-interferon to animals, such as, *e.g.,* Bocci et al. (C06) or Supersaxo et al. (C31), none of the references cited disclose the claimed subject matter which relates to intradermal delivery of α-interferon, wherein delivery of α-interferon to the dermis produces improved systemic pharmacokinetics as compared to subcutaneous administration of α-interferon.

The Statutory Type Provisional Double Patenting Rejection of Claims 22-35 Should be Held in Abeyance Until Indication of Allowable Subject Matter

Claims 22-35 are provisionally rejected under the judicially created doctrine of statutory type double patenting as allegedly being unpatentable over claims 28-41 of copending Application No. 10/487,485 ("the '485 application").

Without acquiescing to the Examiner's rejection, Applicant points out that according to MPEP §804(I)(B), if the provisional double patenting rejections in both applications are

the only rejections remaining in those applications, the Examiner should then withdraw that rejection in one of the applications and permit the application to issue as a patent.

Therefore, Applicant respectfully requests that if the Examiner maintain the present rejection, the Examiner hold this provisional double-patenting rejection in abeyance until such time as relevant claims of the '485 application or the instant application, are allowable.

The Obviousness Type Provisional Double Patenting Rejection of Claims 22-24, 26, and 31 Should be Held in Abeyance Until Indication of Allowable Subject Matter

Claims 22-24, 26, and 31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 2, 4, and 29 of co-pending U.S. Patent Application No. 09/606,909 ("the '909 application"). The Examiner alleges that although the conflicting claims are not identical, they are not patentably distinct because claims 2, 4, and 29 of the '909 application fall entirely within the scope of claims 22-24, 26, and 31 of the instant application.

Without acquiescing to the Examiner's rejection, Applicant points out that according to MPEP §804(I)(B), if the provisional double patenting rejections in both applications are the only rejections remaining in those applications, the Examiner should then withdraw that rejection in one of the applications and permit the application to issue as a patent.

Therefore, Applicant respectfully requests that if the Examiner maintain the present rejection, the Examiner hold this provisional double-patenting rejection in abeyance until such time as relevant claims of the '909 application or the instant application, are allowable.

The Rejection of Claims 22-28 and 30-35 Under 35 U.S.C. § 102 Should Be Withdrawn

Claims 22-28 and 30-35 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Zahn *et al.* 2000 *Biomedical Microdevices* 2(4): 295-305 ("Zahn"). Claims 22-28, 31, and 33-35 further stand rejected under 35 U.S.C. § 102(b) as being anticipated by Henry *et al.* 1998 *J. Pharm Sci* 87(8): 922-5 ("Henry"). The claims have been amended to incorporate the limitations of dependent claim 40 -- wherein the substance to be delivered is α-interferon. Dependent claim 40 was not rejected as anticipated by Henry or Zahn, as neither reference discloses the delivery of α-interferon. Applicant respectfully submits that both Zahn and Henry fail to disclose each and every element of the claimed invention, and thus cannot anticipate the claimed invention.

Thus, Zahn and Henry cannot anticipate the claimed invention and rejection of claims 22-28 and 30-35 under 35 U.S.C. § 102 (b) should be withdrawn.

The Rejection of Claims 22, 29, 36, 38, and 40 Under 35 U.S.C. § 103 Should Be Withdrawn

Pending claim 22 is rejected under 35 U.S.C. § 103(a) as unpatentable over Henry in view of Sato *et. al.* Science 1996; 273(5273): 352-354 ("Sato"). Pending claims 22 and 29 are rejected under 35 U.S.C. § 103(a) as unpatentable over Zahn in view of Sato. Claims 36, 38, and 40 have been cancelled, thus voiding the rejection of these claims. The rejections of the pending claims should be withdrawn for the reasons detailed below.

One of the basic criteria for establishing a prima facie case of obviousness is that the prior art references when combined must teach or suggest all the claim limitations of the pending application. MPEP §2143.03. Furthermore, if an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Pending claim 22 relates to a method of administering α-interferon by delivering α-interferon intradermally through one or more microneedles having a length and outlet suitable for selectively delivering α-interferon into the dermis resulting in improved systemic pharmacokinetics compared to subcutaneous administration. Dependent claim 29 requires that the length of the microneedle ranges from about 0.5 to 1.7 mm.

The Examiner asserts that it would have been prima facie obvious to one of ordinary skill in the art to apply the drug delivery method of Zahn or Henry to the administration of interferon as described by Sato to arrive at the claimed invention. First, neither Henry nor Zahn describe or suggest delivery of α-interferon as required by the pending claims of the instant application. This deficiency is not cured by Sato. Regarding the teachings of Sato, Applicant respectfully points out that the Examiner is incorrect in the interpretation of the reference. Sato *does not* teach administration of genes expressing immunostimulatory proteins such as α-interferon. Rather, Sato relates to vaccine delivery of plasmid DNA that "have been reported to induce production of IFN-α, IFN-β, and IFN-γ..." (see, Sato, col. 3 of page 352). Thus, Sato relates to the delivery of certain types of vaccines that may induce the subject to *produce* interferon, *not the delivery* of interferon to the subject. Therefore, the

suggestion of delivery of α-interferon absent from Zahn and/or Henry is not provided by Sato.

Second, neither Zahn nor Henry describe or suggest intradermal drug delivery as required by the claimed invention. The claimed invention requires delivery through one or more microneedles having a length and outlet suitable for delivery to the intradermal space. Zahn relates to microneedles 7 mm in length - - a needle length too long to target the intradermal compartment (see, *e.g.*, ¶ [0016] of the instant specification). Further, Zahn is devoid of any reference to the delivery of pharmaceutical substances. Henry relates to a disclosure of a multiple needle array device, with a maximum needle length of 150 μm (*see,* Henry at page 923, col. 2), which at best penetrates the outer layer of the skin, the stratum corneum, not the intradermal space. The instant specification teaches that intradermal is intended to mean administration at a depth of at least about 0.3 mm (*see*, *e.g.,* the instant application at ¶ [0016]). The microneedle array described in of Henry contains solid, not hollow, needles designed to puncture the stratum corneum of the skin to improve skin permeability, thus at best achieving topical delivery. Thus, the methods and devices disclosed in either reference fail to teach or suggest intradermal delivery, as required by the pending claims.

Further, the cited art is devoid of any suggestion to improve pharmacokinetic profiles of α-interferon. Neither Henry nor Zahn describe or suggest improved systemic pharmacokinetics. This deficiency is not cured by Sato. Sato relates to gene vaccine delivery and is concerned with the body's immune response to a vaccine -- not systemic pharmacokinetic profiles of the administered vaccine. Unlike drugs, the efficacy and potency of vaccinations are not evaluated using PK studies. The Examiner has improperly attributed parameters and properties of the drug delivery art to the vaccine art. Pharmacokinetic studies are meaningless in the vaccine art as practitioners in this field do not gauge the potency of the vaccine by its ability to be circulated systemically. In fact, as evidenced by the World Health Organization Guideline on Non-Clinical Evaluation of vaccine, pharmacokinetic studies, e.g., determining serum or tissue concentrations of the vaccine are normally not needed and in fact shed no light on the efficacy of a vaccine. Thus, there is no motivation either in the references themselves or in the knowledge of one of ordinary skill in the art to combine the disclosures of either Zahn or Henry, which at best relate to non-intradermal drug delivery, with Sato which relates to vaccine delivery. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where

there is a suggestion found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *MPEP § 2143.01.*

Thus, neither Sato, Henry, or Zahn supply the pharmacokinetic profile element nor the delivery of α-interferon element of the pending claims; therefore, the combinations do not render the claims obvious and the rejection of claims under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

Entry of the foregoing amendments and consideration of the remarks is respectfully requested. The claims are believed to be patentable and free of the art. Early allowance is respectfully requested.

Respectfully submitted, by: Jacqueline Benn
Reg No. 43,492

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Laura A. Corruzzi 30,742

Laura A. Corruzzi (Reg. No.)
JONES DAY
222 East 41st Street
New York, New York 10017
(212) 326-3939